

Notice of Allowability

Application No.

10/553,614

Applicant(s)

HIRAI, MITSU HARU

Examiner

Molly E. Baughman

Art Unit

1637

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to communication filed 10/5/07 and an interview with Che Chereskin on 10/25/07.
2. ☒ The allowed claim(s) is/are 1-9.
3. ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some* c) ☐ None of the:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☒ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

* Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.

THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

4. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.
5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
- (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
- 1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
- (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.
- Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).
6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

- | | |
|--|--|
| 1. <input type="checkbox"/> Notice of References Cited (PTO-892) | 5. <input type="checkbox"/> Notice of Informal Patent Application |
| 2. <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 6. <input checked="" type="checkbox"/> Interview Summary (PTO-413),
Paper No./Mail Date <u>20071025</u> . |
| 3. <input type="checkbox"/> Information Disclosure Statements (PTO/SB/08),
Paper No./Mail Date _____ | 7. <input checked="" type="checkbox"/> Examiner's Amendment/Comment |
| 4. <input type="checkbox"/> Examiner's Comment Regarding Requirement for Deposit
of Biological Material | 8. <input checked="" type="checkbox"/> Examiner's Statement of Reasons for Allowance |
| | 9. <input type="checkbox"/> Other _____ |

EXAMINER'S AMENDMENT

1. An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Che Chereskin on 10/25/07.

The application has been amended as follows:

CLAIM 1:

2. Delete the entire claim 1 and replace with --A nucleic acid probe comprising a 5' end which is labeled with a fluorescent dye, and in which fluorescence of the fluorescent dye decreases upon hybridization, wherein the nucleic acid probe has a 5' end nucleotide complementary to nucleotide number 247 of SEQ ID NO:1 and has a nucleotide sequence complementary to 13 to 30 nucleotides 5' to nucleotide number 247 of SEQ ID NO:1, and wherein the 5' end of the probe is labeled with the fluorescent dye.

CLAIM 7:

3. Delete the entire claim 7 and replace with --A kit for the method as defined in claim 3, comprising a nucleic acid comprising an end which is labeled with a fluorescent dye, and in which fluorescence of the fluorescent dye decreases upon hybridization, wherein the nucleic acid probe has a 5' end nucleotide complementary to nucleotide

number 247 of SEQ ID NO:1 and has a nucleotide sequence complementary to 13 to 30 nucleotides 5' to nucleotide number 247 of SEQ ID NO:1, and wherein the 5' end of the probe is labeled with the fluorescent dye.

4. The following is an examiner's statement of reasons for allowance: Prior art has been found teaching a probe and a method of using the probe, wherein the probe comprises the nucleotide at nucleotide 247 and a sequence 5' to the nucleotide in the nucleotide sequence of SEQ ID NO:1, as well as a probe comprising that of SEQ ID NO: 12 and 13, to detect the S20G mutation of the pancreatic islet amyloid polypeptide, as taught in the instant claims (Lee et al., WO 02/072875). Prior art has also been found teaching methods of designing probes with a 5' labeled cytosine, complementary to one or more guanosine nucleotides in the template sequence, which cause a decrease in fluorescence or quenching of the fluorophore at the 5' end upon hybridization (i.e. without a secondary label or quencher) (Crockett et al., "Fluorescein-Labeled Oligonucleotides for Real-Time PCR: Using the Inherent Quenching of Deoxyguanosine Nucleotides," Analytical Biochemistry, 2001, Vol.290, pp.89-97). Although such sequences and methods are known, the instant probe having a 5' end nucleotide (i.e. cytosine) specifically complementary to nucleotide number 247 of SEQ ID NO:1 (i.e. a guanosine directly adjacent to another guanosine), and 13 to 30 nucleotides 5' to nucleotide number 247 of SEQ ID NO:1, in comparison to other probes of the instant invention also having a 5' end cytosine complementary to a guanosine at

other positions of SEQ ID NO:1, provides an unexpected result of a change in fluorescence intensity that could be analyzed in T_m analysis, which ultimately allows for detection of the mutation during PCR (see pg.12 of the instant specification). Other probes with the same configuration, but having 5' cytosine ends complementary to other positions than nucleotide 247 of SEQ ID NO:1 were not effective in T_m analysis during PCR (i.e. SEQ ID NO:10 and 11 of Figure 1 (i.e. 2 probes on the bottom)).

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Summary

5. Claims 1-9 are allowed.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Molly E. Baughman whose telephone number is 571-272-4434. The examiner can normally be reached on Monday-Friday 8-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Molly E Baughman
Examiner
Art Unit 1637

MEB 11/5/07

Kenneth R. Horlick
KENNETH R. HORLICK, PH.D.
PRIMARY EXAMINER

11/6/07